02 - 2. Classification of receptors

2. Classification of receptors

© SPMM Course 2. Classification of receptors Receptors may be categorized into three categories:

(1) Ligand-gated channels (ionotropic), in which binding of a chemical messenger alters the

probability of opening of transmembrane pores or channels;

(2) Those in which the receptor proteins are coupled to intracellular G proteins as transducing

elements (metabotropic);

(3) Those termed ligand-dependent regulators of nuclear transcription (nuclear receptors). Ionotropic or ion channel receptors result in fast response (GABAA benzodiazepine); G protein coupling (metabotropic) is comparatively a slower process (most antipsychotics, antidepressants). Ion channel receptors are made up of four or five protein subunits making up a pore like structure. The GABA-A receptor's structure is typical of most ligand-gated (ionotropic) receptors [‘doughnut with a hole in the centre’ or ‘rosette’ shaped]. Each protein subunit is a string of amino acids which passes in and out of the cell membrane four times. At the extracellular end of this string is a large N-terminal; this end-chain is thought to mediate GABA-channel interactions. In the middle of the string is a large intracellular loop of amino acids with four sites where phosphorylation occurs. Inhibitory neurotransmitter action leads to the entry of Cl- while excitatory action results in the entry of Ca2+ or other cations. Ionotropic receptors include GABAA, NMDA, the 5HT3 subtype of serotonin receptors. G-protein-coupled metabotropic receptors are proteins that span the cell membrane seven times (serpentine receptors). G protein-coupled receptors act via cyclase mediated second messenger activation (GTP, ATP, etc.). Gs-proteins are stimulatory; Gi-proteins inhibit the adenylate cyclase. A third variant of G-protein receptors acts via phospholipase C. Metabotropic receptors influence protein synthesis eventually thus producing longer lasting effects. Metabotropic receptors include DA receptors, most 5HT receptors except 5HT-3, NEN and neuropeptides including opioid receptors are G coupled. Nuclear receptors such as glucocorticoid receptors are part of a superfamily of receptors that have a cysteine-rich DNA-binding domain, a ligand-binding domain, and a variable amino terminal region. Upon appropriate ligand binding, a nuclear receptor becomes a transcription factor and binds in turn to DNA via zinc fingers. Other nuclear receptors include the receptors for progesterone, androgen, and

1,25dihydroxycholecalciferol (Vitamin D). Many receptors of this family are orphan receptors, for which the ligands are still unidentified. The glucocorticoid receptor is located mainly in the cytoplasm but migrates to the nucleus as soon as it binds its ligand. In contrast, the estrogen and the triiodothyronine (T3) receptors are retained in the nucleus and bind hormones directly in the nucleus itself.

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